National Institute for Health and Care Excellence

FINAL

Thyroid disease: assessment and management

[A] Information for people with thyroid disease

NICE guideline NG145

Qualitative evidence review underpinning recommendations 1.1.1 to 1.1.6 in the guideline

2019

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1 Information for people with thyroid disease

1.1 Review question: What information should people with thyroid disease, their family and carers receive?

1.2 Introduction

We asked the question: What information should people with thyroid disease, their family and carers receive? The NICE guideline on Patient Experience (CG138) has established that people receiving medical care (along with their carers and families) require information about their diagnosis, the course of their medical condition and their choices in regard to treatment. This is in order to control and minimise psychological stress, as well as to provide useful practical advice in managing their disease on a day to day basis and to issue important warnings.

The Thyroid Disease NICE Guideline Committee looked at findings from qualitative studies to see what sort of information and support people with thyroid diseases need. Many people need general information about where their thyroid is and what it does.

However, at present there is no standardised agreed practice for healthcare professionals and people with thyroid disease on who gives the person information, what information is given and when it is given. There are many good sources of information including the NHS Choices website and leaflets (both online and hard copy) from patient groups. Some of these are written by people with thyroid disease, working with endocrinologists and other experts.

1.3 Characteristics table

For full details see the review protocol in Appendix A:.

Table 1: Characteristics of review question

Objective	To identify the types of information that people with thyroid disease benefit from
Population and setting	People who have been diagnosed with thyroid disease, their family, carers or healthcare professionals Strata: people with thyroid disease, family, healthcare professionals, people with hypothyroidism, hyperthyroidism, thyroid enlargement
Context	Evidence reported in qualitative studies relating to the information needs of people with thyroid disease, their family or carers will be extracted. Suggested areas based on the committee experience include: • Investigation • Management • Long-term follow-up • Familial risk of thyroid disease • Advice for women of child-bearing age • Warning signs of thyroid eye disease (excluding management) • Specific risks and benefits of treatment • Uncertainty around adverse effects of treatment • Information around the effects of radiation exposure • Medication adherence and interactions
Review strategy	Synthesis of qualitative research. Results presented in narrative format. Quality of the evidence will be assessed by a GRADE CerQual approach for each review finding.

1.4 Qualitative evidence

1.4.1 Included studies

Three qualitative studies were included in the review;[2, 3, 6] these are summarised in Table 2 below. Key findings from these studies are summarised in Section 1.4.2 below. See also the study selection flow chart in Appendix C:, study evidence tables in Appendix D:, and excluded studies lists in Appendix G:.

1.4.2 Excluded studies

See the excluded studies list in Appendix H:.

1.4.3 Summary of qualitative studies included in the evidence review

Table 2: Summary of studies included in the review

Study	Design	Population	Research aim	Comments
Dew 2017 [2]	Semi-structured face-to-face interviews and grounded theory analysis	Patients with overt hypothyroidism established on levothyroxine ≥12 months (n=27); n=15 with thyroid stimulating hormone (TSH) within reference range (0.4-4.0 mU/L)	To explore the experiences, attitudes and perceptions of patients with hypothyroidism towards their treatment, to explore the behavioural factors that may contribute to suboptimal treatment.	Hypothyroidism focused
Dew 2018 [3]	Semi-structured interviews (majority face to face, on telephone) and grounded theory analysis	Health professionals from general practice and community pharmacies (n= 16), comprising 9 GPs, 4 pharmacists, 2 practice nurses and 1 nurse practitioner, recruited through the National Institute for Health Research (NIHR) Clinical Research Network	To investigate the attitudes and perceptions of health professionals towards management of hypothyroidism, to determine the clinical management and behavioural factors that may influence the adequacy of thyroid hormone replacement in patients with hypothyroidism.	Hypothyroidism focused
Ingoe 2018 [6]	Semi-structured interviews, thematic and grounded theory analysis	Patients aged 80 and over with a diagnosis of primary hypothyroidism (n=18) who had agreed to randomisation on the SORTED 1a RCT ('Accepters', n=11) or from a group of patients who had declined the trial ('Decliners', n=7)	To explore the experience of hypothyroidism in older people and examine how this may influence their understanding and acceptance of diagnosis, treatment with Levothyroxine and the monitoring process.	Hypothyroidism focused Interviews were conducted as part of a feasibility RCT examining the impact of reducing LT4 dose in patients aged 80 and over with an existing diagnosis of hypothyroidism, to explore barriers and facilitators to recruitment and retention of older patients in clinical trials; Data saturation was based on the RCT objectives.

See Appendix D: for full evidence tables.

1.4.4 Qualitative evidence synthesis

1.4.4.1 Narrative summary of review findings

TSH targets & symptoms

Patients often appear to be unsure of the relationship of their symptoms to their thyroid disease. Blood tests that are within normal parameters are perceived to indicate a euthyroid state regardless of the presence of symptoms, and patients perceive that blood samples rather than symptom checks determine management. Some patients report feeling well regardless of whether their TSH levels are in range or not while others continue to feel unwell despite normal TSH results. As a result, patients report feeling that their symptoms cannot be managed or that symptoms are being ignored by clinicians or are assumed to be unrelated to their thyroid condition.

Explanation of quality assessment: minor methodological limitations; minor concerns about coherence; no concerns about relevance; minor concerns about adequacy. Overall assessment of confidence was moderate due to concerns about coherence and adequacy.

Non-specific nature of symptoms

People reported that due to the non-specific nature of thyroid symptoms their diagnoses were sometimes delayed or there was uncertainty regarding the cause of their symptoms and whether they could be directly related to hypothyroidism. The overlap between hypothyroidism symptoms and natural ageing also left some people questioning the veracity of their diagnosis and the need for treatment or led others to attribute symptoms such as tiredness and memory problems to ageing. GPs agreed on the non-specific nature of symptoms which overlap with numerous conditions and often results in a variety of symptoms experienced by patients being attributed to their thyroid.

Explanation of quality assessment: minor methodological limitations; very minor concerns about coherence; no concerns about relevance; minor concerns about adequacy. Overall assessment of confidence was moderate due to the concerns about adequacy.

Medication interactions

Health professionals reported that thyroid medication may interact with other medication, dietary and lifestyle factors including alcohol, coffee and smoking and this may influence its absorption. This potential interaction may explain an elevated TSH in cases where patients adhere to medication. Some patients reported receiving thyroid treatment promoting advice from their pharmacists such as timing of medication, avoiding food and other medication.

Explanation of quality assessment: minor methodological limitations; very minor concerns about coherence; no concerns about relevance; minor concerns about adequacy. Overall assessment of confidence was moderate due to the concerns about adequacy.

Importance of adherence

Health professionals reported good adherence to medication was important for optimal treatment and incorrect adherence was in their experience the main reason for inadequate thyroid control. Some patients felt they needed to take their levothyroxine to prevent the symptoms of hypothyroidism. The lack of information about medication including the reasons for potential alterations in dosage left some patients with doubts about the need for medication.

Explanation of quality assessment: minor methodological limitations; moderate concerns about coherence; no concerns about relevance; minor concerns about adequacy. Overall assessment of confidence was low due to the concerns about coherence.

Barriers to optimal thyroid replacement

People's understanding of treatment and the perceived benefits of a change in dose are likely to influence the extent to which they adhere to it. A lack of an understanding may lead to incorrect adherence with some patients taking more medication than prescribed to alleviate symptoms of tiredness or to lose weight. Lack of consensual decision making between patients and their GPs when patients feel there is room for improvement of their treatment by the GP and overreliance on TSH within reference range as the sole measure of adequate hormone replacement are perceived barriers to optimising thyroid control.

Explanation of quality assessment: minor methodological limitations; moderate concerns about coherence; no concerns about relevance; minor concerns about adequacy. Overall assessment of confidence was moderate due to concerns about coherence.

Availability of information

Health professionals perceive that patients research their condition online and get information from online forums. Thus professionals tend to provide a limited amount of information in verbal form and rarely use written information leaflets. Patients report receiving limited information, particularly about their symptoms and treatment and not being given information at the time of their diagnosis. Often due to time constraints, professionals report directing patients to online resources such as patient.co.uk. Patients report seeking information from informal sources to fully understand diagnostic decisions and treatment changes, such as the internet which they felt could be inaccurate and provoke anxiety leading them to put off researching.

Explanation of quality assessment: minor methodological limitations; very minor concerns about coherence; no concerns about relevance; no concerns about adequacy. Overall assessment of confidence was high.

Risks of over or under treatment

Health professionals perceive that patients lack awareness of the risks of over and under treatment. Indeed patients appeared to have poor knowledge of the consequences of poor treatment adherence or the risks associated with being out of the therapeutic treatment range. This may lead to incorrect adherence as patients have been reported by health professionals to take more than prescribed aiming to lose weight or to alleviate symptoms such as tiredness while the elderly tend to perceive increased doses as advantageous. Health professionals' awareness of the cardiac complications and increased risk for fractures associated with overtreatment and their perception of patients' lack of it prevents them from over treating patients, especially the elderly.

Explanation of quality assessment: minor methodological limitations, very minor concerns about coherence; no concerns about relevance; minor concerns about adequacy. Overall assessment of confidence was moderate due to the minor concerns about adequacy.

1.4.5 Qualitative evidence summary

Table 3: Summary of evidence

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Findings**	**Criteria**	**Rating**	**Overall assessment of confidence**
TSH targets & symptoms					
2	Semi-structured interviews with thematic and grounded theory analysis (2 studies)	Normal blood tests in the presence of symptoms, feeling well regardless of TSH levels or unwell despite normal TSH results cause uncertainty in patients about the relationship between symptoms and thyroid disease.	Limitations	Minor limitations	MODERATE
			Coherence	Minor concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy	
Non-specific symptoms					
3	Semi-structured interviews with thematic and grounded theory analysis and semi-structured interviews with grounded	The non-specific nature of thyroid symptoms meant that diagnosis was delayed for some people and left them questioning the veracity of the condition and the need for treatment, led them to attribute a number of symptoms on their thyroid or caused uncertainty about whether various symptoms they experienced could be directly related to their thyroid.	Limitations	Minor limitations	MODERATE
			Coherence	Very minor concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy	

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Findings**	**Criteria**	**Rating**	**Overall assessment of confidence**
	theory analysis (3 studies)				
Medication interactions					
2	Semi-structured interviews and grounded theory analysis (2 study)	The interactions of thyroid medication with other medication, comorbidities and dietary or lifestyle factors may explain suboptimal thyroid replacement despite medication compliance.	Limitations	Minor limitations	MODERATE
			Coherence	Very minor concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy	
Importance of adherence					
3	Semi-structured interviews with grounded theory analysis and semi-structured interviews with thematic and grounded theory analysis	Good adherence to medication is important for optimal treatment with patients reporting the need for treatment to prevent symptoms but a lack of information about medication may cast doubt about the need for it.	Limitations	Minor limitations	LOW
			Coherence	Moderate concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy	

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	Design	Findings	Criteria	Rating	Overall assessment of confidence
	(3 studies)				
Barriers to optimal thyroid replacement					
3	Semi-structured interviews with grounded theory analysis and semi-structured interviews with thematic and grounded theory analysis (3 studies)	Patients' understanding of treatment may influence treatment adherence while lack of shared decision making between patients and GPs and overreliance on TSH levels as a measure of adequate thyroid replacement, present barriers to optimal treatment.	Limitations	Minor limitations	MODERATE
			Coherence	Moderate concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy	
Availability of information					
3	Semi-structured interviews with grounded theory analysis and semi-structured interviews	A limited amount of verbal information is provided with patients often turning to online resources, which are often perceived as inaccurate, to understand their thyroid condition and its management.	Limitations	Minor limitations	HIGH
			Coherence	Very minor concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	Design	Findings	Criteria	Rating	Overall assessment of confidence
	with thematic and grounded theory analysis (3 studies)				
Risks of over or under treatment					
3	Semi-structured interviews with grounded theory analysis and semi-structured interviews with thematic and grounded theory analysis (3 studies)	Health professionals but not patients appear to be aware of the risk of overtreatment which makes the former less likely to overtreat and the latter likely to occasionally take more than prescribed.	Limitations	Minor limitations	MODERATE
			Coherence	Minor concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy	

1.5 Economic evidence

The committee agreed that health economic studies would not be relevant to this review question, and so health economic evidence relating to this question was not sought.

1.6 Evidence statements

1.6.1 Qualitative evidence statements

- Three qualitative studies suggested the following about the information needs of people with thyroid disease, their family, carers or health professionals:
  - Moderate quality evidence from 2 studies suggested that people need information about TSH targets and symptoms to alleviate their uncertainty about the relationship between their symptoms and their thyroid disease.
  - Moderate quality evidence from 3 studies highlighted that it is important to have information on the non-specific nature of thyroid symptoms to prevent potential delays in diagnosis, help people understand their condition and the need for treatment and prevent them from attributing a number of symptoms on their thyroid.
  - Moderate quality evidence from 2 studies highlighted that information about medication interactions should be given to patients, to prevent interacting dietary and lifestyle factors that may be influencing absorption from leading to suboptimal thyroid replacement in spite of medication adherence.
  - Moderate quality evidence from 3 studies highlighted the importance of giving people information about the importance of good medication adherence to enable optimal treatment and eliminate potential doubt in regards to the need for medication.
  - Low quality evidence from 3 studies highlighted the importance of informing people (health professionals) of barriers to optimal thyroid replacement such as patient's understanding of treatment, overreliance on TSH levels and lack of consensual decision making to encourage information provision and facilitate adherence.
  - High quality evidence from 3 studies highlighted the sources of information that patients require and their need for further information as the lack of sufficient verbal information provided by health professionals leads patients to online and potentially inaccurate resources in order to gain an understanding of their thyroid condition and its management.
  - Moderate quality evidence from 3 studies highlighted the importance of providing people with information about the risks of over and under treatment, as patient's lack of such awareness may often lead them to take more than prescribed to alleviate symptoms.

1.7 The committee's discussion of the evidence

1.7.1 Interpreting the evidence

1.7.1.1 The quality of the evidence

The evidence quality ranged from high to low, the majority being of moderate quality due to mainly minor concerns about the coherence and adequacy of the findings. In particular, issues concerning the richness of data, depth of analysis and consistency of the findings across studies limited our confidence in the evidence. The findings were all applicable to the population and setting of this review. The studies were all conducted on a population with hypothyroidism or in health professionals supporting people with hypothyroidism. Participants of one study were older adults aged 80 and over. The committee were in agreement that the themes presented were consistent with their own experience with patient requests and with existing comments from stakeholders. Based on a combination of the evidence in the review, consensus and their clinical experience the committee agreed on the information that people with thyroid disease need.

1.7.1.2 Findings identified in the evidence synthesis and raised in committee discussion

General

Evidence from two studies suggested that people with thyroid disease need clarification on the relationship between TSH and their symptoms. The committee agreed that symptoms and thyroid function tests may not always be concordant, with people with thyroid disease, possibly experiencing or not experiencing symptoms in the presence of abnormal TSH. Within this framework, the committee thought it would be important to inform people that the goal of treatment is to have both well-being and TSH levels restored.

It was raised that discordance between thyroid function and the experience of symptoms is often a cause of under treatment such as when people are asymptomatic, they are less likely to engage with healthcare services. The committee emphasised that people should be made aware that treatment may be required even in the absence of symptoms due to the long term health consequences of untreated thyroid disease.

The committee raised that a considerable number of people with thyroid disease whose TSH is within reference range continue to feel unwell, noting that changes in treatment may be beneficial in terms of symptoms for those people. Hence it was agreed that information on the impact of treatment adjustments on symptom improvement in the presence of normal TFTs should be given.

It was emphasised that due to the underlying physiology of thyroid hormones it takes some time for changes in treatment to have an impact on thyroid function. Hence, the committee agreed that people with thyroid disease should be made aware of this to prevent potential frustration due to the persistence of symptoms despite treatment changes and to help people understand whether symptoms or their changes are truly thyroid related.

The committee highlighted the fact that people with thyroid disease as well as their carers often lack basic knowledge as to what the thyroid is and how it works and the committee agreed people need to be made aware of key issues including: the role and function of the thyroid gland, risks of over and under treatment, the exact medication taken, monitoring needs, information as to when to seek help and on the impact of thyroid disease and thyroid medication on fertility and pregnancy. It was noted that a lack of information coming from health professionals may often lead to misinformation with people with thyroid disease turning to potentially unreliable sources to get the information they need. Within this framework, it was highlighted that people could use direction towards legitimate and useful sources of information such as NHS choices to avoid misinformation.

Hypothyroidism

Evidence from three studies suggested that it is important to provide people information on medication interactions. The committee noted that thyroid medication interacts with other medication, nutrition supplements and tea or coffee and that for optimal thyroid replacement it should be taken in the morning or evening on an empty stomach. They agreed that people with hypothyroidism, should be made aware of drug interactions with levothyroxine and informed on when best to take it.

Evidence from three studies suggested people need information on thyroid medication and the importance of adherence as well as the risks of over and under treatment. Evidence from 3 studies also highlighted a lack of understanding of treatment as a barrier to optimal thyroid replacement and a lack of verbal information people with thyroid disease faced. Committee lay members agreed that people are sometimes not given enough verbal or written information on their thyroid condition and that they could use more information in the form of patient leaflets.

Thyrotoxicosis

No direct evidence on the information needs of people with thyrotoxicosis, thyroid enlargement, their families or carers was identified. However, the guideline committee agreed that the evidence highlighted certain key areas that people with thyroid disease require information on and highlighted the lack of verbal and written information currently given by health professionals.

In absence of evidence regarding the information needs of people with thyrotoxicosis, the committee agreed to make recommendations based on consensus for those people. It was agreed that it was important to provide people with thyrotoxicosis with written and verbal information on the different causes of their condition and the consequences of untreated thyrotoxicosis. It was raised that people with thyrotoxicosis may not receive full information on the advantages, disadvantages and uncertainties surrounding their treatment options. This is particularly critical for thyrotoxicosis where people must make decisions between distinct treatment modalities. The committee agreed that they should hence be given information on benefits and risks of all treatment modalities for example the side effects of antithyroid drugs, the specific implications of RAI, as well as information on radiation protection for carers and information on the implications and risks of surgery such as potential voice changes and hypoparathyroidism. The committee highlighted that it is particularly important to give people with thyrotoxicosis information on the risk and impact of thyroid eye disease (TED) although management of this was not a focus of the guideline.

Enlargement

The committee agreed it was important for people with thyroid enlargement to know the possible causes of their condition and that both goitre and nodules are common and rarely cancerous. They also felt it was important that although enlargement is rarely cancerous people are aware of red flag symptoms for malignancy or dangerous compression such as a hoarse voice and swallowing difficulties as well as their treatment options.

1.7.2 Cost effectiveness and resource use

Cost effectiveness evidence was not sought, as this was a qualitative review about information needs of people with thyroid disease.

The recommendations provide guidance regarding the type of information and support that should be provided to people with thyroid disease in line with the general principles of provision of information already established in the existing NICE Patient Experience Guideline and so were not considered likely to have a substantial resource impact over and above this. Where this level of information is not currently being provided there may be additional resource use for example if longer or more consultations are required or a written material needs to be produced. Better information may however also lead to downstream benefits for the patient and/or reductions in resource use, for example if it leads to medication being taken more appropriately.

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Appendices

Appendix A: Review protocols

Table 4

ID	Field	Content
I	Review question	What information should people with thyroid disease, their family and carers receive?
II	Type of review question	Qualitative A review of health economic evidence related to the same review question was conducted in parallel with this review. For details see the health economic review protocol for this NICE guideline.
III	Objective of the review	To identify the types of information that people with thyroid disease benefit from
IV	Eligibility criteria – population / disease / condition / issue / domain	Studies will be included if they seek the viewpoint of people who have been diagnosed with thyroid disease, their family, carers or healthcare professionals
V	Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	• Not applicable
VI	Eligibility criteria – comparator(s) / control or reference (gold) standard	• Not applicable
VII	Outcomes and prioritisation	Evidence reported in qualitative studies relating to the information needs of people with thyroid disease, their family or carers will be extracted. Themes identified in the evidence will be used to compile the overall qualitative evidence synthesis, however suggested areas based on the committee experience include: • Investigation • Management • Long term follow-up • Familial risk of thyroid disease • Advice for women of child-bearing age • Warning signs of thyroid eye disease (excluding management) • Specific risks and benefits of treatment • Uncertainty around adverse effects of treatment • Information around the effects of radiation exposure • Medication adherence and interactions

VIII	Eligibility criteria – study design	Qualitative interview and focus group studies (including studies using grounded theory, phenomenology or other appropriate qualitative approaches); quantitative data from questionnaires will only be considered if insufficient qualitative evidence is identified
IX	Other inclusion exclusion criteria	Qualitative studies will be added to the review until themes within the analysis became saturated; i.e. studies will only be included if they contribute towards the development and richness of existing themes or to the development of new themes
X	Proposed sensitivity / subgroup analysis, or meta-regression	**Stratifications** • People with thyroid disease vs family vs healthcare professionals • People with hypothyroidism, hyperthyroidism, thyroid enlargement
XI	Selection process – duplicate screening / selection / analysis	• A sample of at least 10% of the abstract lists were double-sifted by a senior research fellow and discrepancies rectified, with committee input where consensus could not be reached, for more information please see the separate Methods report for this guideline.
XII	Data management (software)	• Endnote was used for bibliography, citations, sifting and reference management
XIII	Information sources – databases and dates	• Medline, Embase, CINAHL, PsycINFO
XIV	Identify if an update	Not an update
XV	Author contacts	https://www.nice.org.uk/guidance/indevelopment/gid-ng10074
XVI	Highlight if amendment to previous protocol	Not an amendment
XVII	Search strategy – for one database	For details please see Appendix B:
XVIII	Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as Appendix D: of the evidence report.
XIX	Data items – define all variables to be collected	For details please see evidence tables in Appendix D: (clinical evidence tables) or H (health economic evidence tables).
XX	Methods for assessing bias at outcome / study level	The Critical Appraisal Skills Programme (CASP) Qualitative checklist was used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
XXI	Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual.

XXII	Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the separate Methods report for this guideline.
XXIII	Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
XXIV	Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
XXV	Rationale / context – what is known	For details please see the introduction to the evidence review.
XXVI	Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by Sarah Fisher in line with section 3 of Developing NICE guidelines: the manual. Staff from NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details please see Developing NICE guidelines: the manual.
XXVII	Sources of funding / support	NGC is funded by NICE and hosted by the Royal College of Physicians.
XXVIII	Name of sponsor	NGC is funded by NICE and hosted by the Royal College of Physicians.
XXIX	Roles of sponsor	NICE funds NGC to develop guidelines for those working in the NHS, public health and social care in England.
XXX	PROSPERO registration number	Not registered

Table 5: Health economic review protocol

Review question	**All questions – health economic evidence**
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence.

	• Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see Appendix B: below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2003, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[8] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2003 or later but that depend on unit costs and resource data entirely or predominantly from before 2003 will be rated as 'Not applicable'. • Studies published before 2003 will be excluded before being assessed for

	applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2018 https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869

For more detailed information, please see the Methodology Review.

B.1 Clinical search literature search strategy

Searches for patient views were run in Medline (OVID), Embase (OVID), CINAHL, Current Nursing and Allied Health Literature (EBSCO) and PsycINFO (ProQuest). Search filters were applied to the search where appropriate.

Table 6: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 07 January 2019	Exclusions Qualitative studies
Embase (OVID)	1974 – 07 January 2019	Exclusions Qualitative studies
CINAHL, Current Nursing and Allied Health Literature (EBSCO)	Inception – 07 January 2019	Qualitative studies
PsycINFO (ProQuest)	Inception – 07 January 2019	Qualitative studies

Medline (Ovid) search terms

1.	exp thyroid diseases/
2.	hyperthyroid*.ti,ab.
3.	hypothyroid*.ti,ab.
4.	thyrotoxicosis.ti,ab.
5.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/

20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language
27.	"patient acceptance of health care"/ or exp patient satisfaction/ or consumer health information/ or needs assessment/
28.	Patient Education as Topic/ or exp patients/ or exp family/ or caregivers/ or patient preference/
29.	((information* or advice or advising or advised or support*) adj3 (patient* or need* or requirement* or assess* or seek* or access* or disseminat*)).ti,ab.
30.	(information* adj2 support*).ti,ab.
31.	((client* or patient* or user* or carer* or consumer* or customer* or parent* or famil* or spouse*) adj2 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience or experiences or opinion* or preference* or focus group*)).ti,ab.
32.	or/27-31
33.	Qualitative research/ or Narration/ or exp Interviews as Topic/ or exp "Surveys and Questionnaires"/ or Health care surveys/
34.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
35.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*).ti,ab.
36.	or/33-35
37.	26 and 32 and 36

Embase (Ovid) search terms

1.	exp thyroid diseases/
2.	hyperthyroid*.ti,ab.
3.	hypothyroid*.ti,ab.
4.	thyrotoxicosis.ti,ab.
5.	(thyroid adj3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*)).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	nonhuman/

17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	limit 23 to English language
25.	patient attitude/ or patient preference/ or patient satisfaction/ or consumer attitude/ or needs assessment/
26.	patient information/ or consumer health information/ or patients/ or family/ or caregivers/
27.	((information* or advice or advising or advised or support*) adj3 (patient* or need* or requirement* or assess* or seek* or access* or disseminat*)).ti,ab.
28.	(information* adj2 support*).ti,ab.
29.	((client* or patient* or user* or carer* or consumer* or customer* or parent* or famil* or spouse*) adj2 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience or experiences or opinion* or preference* or focus group*)).ti,ab.
30.	patient education/
31.	or/25-30
32.	health survey/ or exp questionnaire/ or exp interview/ or qualitative research/ or narrative/
33.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
34.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*).ti,ab.
35.	or/32-34
36.	24 and 31 and 35

CINAHL (EBSCO) search terms

S1.	(MH "Thyroid Diseases+")
S2.	hyperthyroid*
S3.	hypothyroid*
S4.	thyrotoxicosis
S5.	(thyroid n3 (swell* or dysfunction* or enlarg* or nodule* or node* or disease* or condition* or disorder*))
S6.	s1 or s2 or s3 or s4 or s5
S7.	(MH "Consumer Satisfaction+") OR (MH "Patient Education") OR (MH "Health Education")
S8.	((information* or advice or advising or advised or support*) n3 (patient* or need* or requirement* or assess* or seek* or access* or disseminat*))
S9.	(information* n2 support*)
S10.	((client* or patient* or user* or carer* or consumer* or customer*) n2 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience or experiences or opinion*))
S11.	S7 OR S8 OR S9 OR S10
S12.	(MH "Qualitative Studies+")

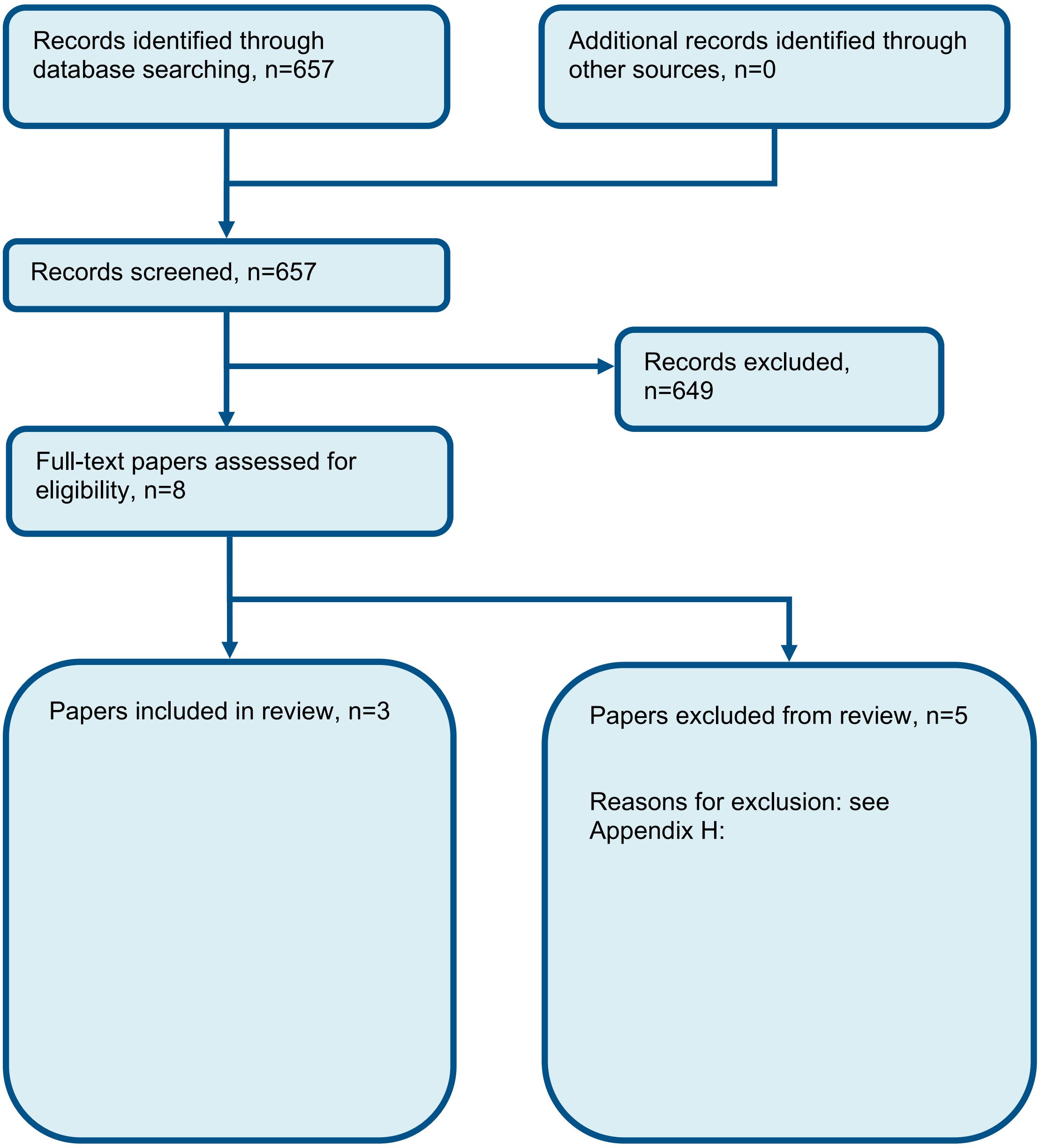
S13.	(MH "Qualitative Validity+")
S14.	(MH "Interviews+") OR (MH "Focus Groups") OR (MH "Surveys") OR (MH "Questionnaires+")
S15.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*)
S16.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* n3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*)
S17.	S12 OR S13 OR S14 OR S15 OR S16
S18.	S6 AND S11 AND S17
	Limit to English language

PsycINFO (ProQuest) search terms

1.	(MAINSUBJECT.EXACT.EXPLODE("Thyroid Disorders") OR TI,AB(HYPERTHYROID* OR HYPOTHYROID* OR THYROTOXICOSIS) OR TI,AB(THYROID NEAR/3 (SWELL* OR DYSFUNCTION* OR ENLARG* OR NODULE* OR NODE* OR DISEASE* OR CONDITION* OR DISORDER*))) AND (SU.EXACT("Client Education") OR SU.EXACT.EXPLODE("Client Attitudes") OR TI,AB((information* OR advice OR advising OR advised OR support*) NEAR/3 (patient* OR need* OR requirement* OR assess* OR seek* OR access* OR disseminat*)) OR TI,AB(information* NEAR/2 support*) OR TI,AB((client* OR patient* OR user* OR carer* OR consumer* OR customer*) NEAR/2 (attitud* OR priorit* OR perception* OR preferen* OR expectation* OR choice* OR perspective* OR view* OR satisfact* OR inform* OR experience OR experiences OR opinion*))) AND ((su.exact.explode("qualitative research") or su.exact("narratives") or su.exact.explode("questionnaires") or su.exact.explode("interviews") or su.exact.explode("health care services") or ti,ab(qualitative or interview* or focus group* or theme* or questionnaire* or survey*) or ti,ab(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* near/3 analys*) or theoretical-sampl* or purposive-sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*)))
	Limit to English language

Appendix C: Qualitative evidence selection

Figure 1: Flow chart of qualitative study selection for the review of information



Appendix D: Qualitative evidence tables

Study	Dew 2017 [2]
Aim	To explore the experiences, attitudes and perceptions of patients with hypothyroidism towards their treatment, to explore the behavioural factors that may contribute to suboptimal treatment.
Population	Patients with overt hypothyroidism established on levothyroxine for ≥ 12 months, recruited through 9 primary care practices in Northumberland and Tyne and Wear by NIHR Clinical Research Network: North East and North Cumbria via posted study packs containing an invitation letter and information sheet. Purposive sampling was used to identify participants from both rural and urban areas, and large and small GP practices, and achieve a maximum variation sample. Theoretical sampling was then used to test emerging categories and themes which proceeded until data saturation was achieved. n=27; male: 9, female: 18; age range 30 to 89 years; 15 patients had TSH levels within reference range (0.4-4.0 mU/L); 12 had TSH levels outside the reference range.
Setting	Patients were residing in Northumberland and Tyne and Wear, UK. Interviews were conducted at the patient's home with the exception of 4 patients who preferred to be interviewed at their GP's surgery, 2 patients at the University of Sunderland and one at their place of work.
Study design	Qualitative interview study
Methods and analysis	In-depth semi-structured interviews were conducted face to face, by the same researcher using an initial topic guide used to explore questions related to the study such as: 'what do you understand about how your thyroid is controlled?', 'Are you aware of any consequences of poor control ?' , which was revised as the study progressed. All interviews were audio recorded and transcribed verbatim and lasted around 45 minutes with only the researcher present except for two occasions where family members were present and contributed. Data collection and analysis were conducted in parallel. Interview data were open coded and then analysed using constant comparison. Themes emerging from the data informed questioning in subsequent interviews. Selective coding was used to identify the core categories and themes. In-depth data analysis was conducted by two researchers and a third researcher was involved in the overall explanation of the data. Emergent themes were mapped to the constructs of the Health Belief Model (HBM). Transcripts were returned to participants for comments and no patients asked for any changes.
Findings	**Symptoms**
	a) Symptom experience: Patient perception of threat of disease was strongly linked to their experience of symptoms prior to diagnosis with patients who had not experienced symptoms being unfamiliar with the typical symptoms of hypothyroidism and having low perceived susceptibility to and severity of the disease.

Study	Dew 2017 [2]
	Thyroid function
	Generally patients had poor knowledge of thyroid function.
	Treatment
	a) (Benefits of) Treatment adherence: Patients felt they needed to take their levothyroxine to prevent the symptoms of hypothyroidism.
	b) Risks of overtreatment: patients had poor knowledge of thyroid function, the consequences of poor treatment adherence, or the risks associated with being out of the therapeutic treatment range.
	Barriers to optimal thyroid hormone replacement
	a) Normal TSH: Patients that had normal TSH result but felt unwell through that their symptoms were being ignored by their GP or assumed them to be unrelated to their thyroid condition and felt that their good TSH result presented a barrier to optimising their treatment. Patients that felt unwell also believed that TSH levels were too crude a measure to gauge optimal thyroid hormone replacement.
	b) Lack of consensual decision making: The GP or endocrinologist was generally seen as responsible for achieving adequate thyroid hormone replacement, rather than patients themselves. Some patients reported that they felt there was lack of consensual decision making between them and their GP, and this may present a barrier to optimising thyroid control if patients felt their GP could improve their treatment.
	c) Symptom uncertainty: Patients' uncertainty regarding the cause of their symptoms may present a barrier to further discussion with their GP to address symptoms and improve well-being. Patients perceived that tiredness and memory problems could be due to aging, inadequate sleep, or from having a long day rather than specifically related to their hypothyroidism. Patients with symptoms such as cold extremities and dry skin felt that they always had these problems and so were unsure if they could relate it directly to their thyroid. The majority felt their thyroid was the cause of their symptoms, however two patients perceived that symptoms might be attributable to a health problem other than hypothyroidism
	Availability of information
	a) Lack of verbal information: Although some patients recall receiving a leaflet, generally, they did not remember very much about it. Some patients described that they had done their own research in an attempt to gain information.
	b) Some patients reported receiving thyroid treatment promoting advice from their pharmacists such as regarding timing of medication, avoiding food and other medication.
	Barriers to information
	a) Information complexity: poor patient knowledge was exacerbated by the complexity of the information presented, and therefore felt that researching on the internet could be inaccurate and could provoke anxiety and were often put off researching.
Limitations and	Moderate limitations due to role of the researcher, data collection and data richness.

Study	**Dew 2017** [2]
applicability of evidence	Minor concerns over applicability due to the research aim.

Study	**Dew 2018** [3]
Aim	To investigate the attitudes and perceptions of health professionals towards management of hypothyroidism that contributes to the suboptimal treatment of hypothyroidism in general practice, to determine the clinical management and behavioural factors that may influence the adequacy of thyroid hormone replacement in patients with hypothyroidism.
Population	Health professionals recruited through the NIHR Clinical Research Network: North East and North Cumbria and local professional networks via mail and email. Purposive sampling was used to recruit participants from both rural and urban areas to provide an initial maximum variation sample. To test emerging themes, theoretical sampling was used thereafter until data saturation was achieved and no new themes were forthcoming. n= 16; male: 4, female: 12; mean age: 44 years (range: 25-60); 6 participants working in rural areas, 10 participants working in urban areas; 9 GPs (5 working in urban areas, 4 in rural areas) qualified for 10-36 years, 4 pharmacists (P) (all working on urban areas) qualified for 2-15 years, 2 practice nurses (N) (1 working on rural area, one working on urban area) both qualified for 40 years, 1 nurse practitioner (NP) working in rural area, qualified for 35 years.
Setting	Health professionals were from general practice and community pharmacies in the counties Northumberland, Tyne and Wear, Stockton-On-Tees and North Cumbria, North of England. Most interviews were conducted at the participants' place of work or the University of Sunderland.
Study design	Qualitative interview study
Methods and analysis	Individual semi-structured interviews were conducted between March and August 2016. Most interviews were conducted face to face at the participant's place of work or the University of Sunderland; one GP was interviewed at home and one was interviewed by telephone. All interviews were conducted by the same researcher (RD) using an initial semi structured topic guide examining the interviewee's perceived role in the management of patients with hypothyroidism, including aspects of management such as: How often do you check thyroid function tests? What are the main influences that you see that contribute to patients struggling to control their hypothyroidism? Interviews lasted approximately 45 minutes. Grounded theory approach was used and themes from initial interviews were explored and developed in subsequent interviews and were mapped to the constructs of the Theory of Planned Behaviour (TPB) which describes the association between an individual's beliefs and their behaviour by considering the influence of their attitude towards a particular behaviour, subjective norms and perceived

Study	Dew 2018 [3]
	behavioural control. Interviews were audio recorded and transcribed verbatim and analysis was performed using Microsoft Word 2010. Open coding of transcripts preceded the categorisation of data and as the interviews progressed, themes emerging from the data were tested in subsequent interviews. Notes made by RD after the interviews were considered during analysis and data analysis occurred concurrently with the interviews and constant comparison and iterative analysis of the interview data allowed for development and remodelling of themes until data saturation was achieved. Coding was performed by RD and in-depth data analysis and negotiation of themes were conducted by RD, KK and SW. Transcripts were returned to participants for comments and corrections but now feedback was received.
Findings	**Symptoms**
	a) Health professionals felt that the symptoms of hypothyroidism were non-specific and overlapped with a number of clinical conditions. They perceived that patients often feel that their thyroid is accountable for many symptoms, particularly weight gain and tiredness.
	Management
	a) Blood tests: Health professionals felt that providing patients with (verbal) information about the importance of blood tests can enable good thyroid management
	Treatment
	a) Medication adherence: GPs felt they were mainly responsible for a patient's treatment, but stressed that good medication adherence by patients was important for optimal treatment.
	b) Factors interfering with medication: GPs and pharmacists highlighted that in cases where patients have an elevated TSH but report they are compliant with their medication, it may be that other medication may be affecting the absorption of levothyroxine. Health professionals also felt that stress, diet, alcohol, coffee, smoking, having a busy lifestyle, comorbidities, other medications, mental health, learning disabilities, deafness and dementia could all have an effect on optimal thyroid hormone replacement. Pharmacists described the need to avoid multivitamins, iron containing drugs, indigestion remedies and coffee. However, health professionals generally perceived they had lack of in depth knowledge of medication interaction.
	c) Risks (and Benefits) of overtreatment: Pharmacists mostly felt that patients were unaware of the risks of under-treatment or overtreatment with levothyroxine. GPs and nurses were conscious of the cardiac complications associated with giving a patient too much levothyroxine too quickly. Extra caution was described when treating the elderly where the risks of fractures may be high. Most GPs and the NP were not prepared to overtreat patients with levothyroxine due to the associated risks.
	d) Incorrect adherence: Health professionals believed that taking too much or too little levothyroxine was the main reason for inadequate thyroid control. They believed that poor levothyroxine adherence was the main reason patients struggle to lower TSH levels. Additionally the majority of health professionals said they had experienced a small proportion of patients who would take more levothyroxine than prescribed to alleviate symptoms of tiredness or in an attempt to lose weight.
	Forms of information provision

Study	**Dew 2018** [3]
	a) Generally health professionals provided verbal information about hypothyroidism and the importance of blood tests. They perceived that patients researched their own condition getting information from online forums, or they would use leaflets from, or direct patients to patient.co.uk
	Barriers to information
	b) Time constraints: GPs and pharmacists felt that the information exchanged with patients is limited by time restrictions, which may often be a result of workload limiting the time available to give advice to patients, with most professionals assuming that patients would research their condition online. Written information leaflets were rarely provided to patients.
	c) Access to patient data: Pharmacists felt they could provide limited advice due to their lack of access to patient medical records and that they could only advise depending on a patient's account of their TSH results and medications. They felt that access to TSH results would save time and inaccuracies in advice they give.
Limitations and applicability of evidence	Minor limitations due to role of the researcher Minor concerns over applicability due to the research aim.

1

Study	**Ingoe 2018** [6]
Aim	Original aim: To explore barriers and facilitators to recruitment and retention of older patients in clinical trials; Incidental aim: To explore the experience of hypothyroidism in older people and examine how this may influence their understanding and acceptance of diagnosis, treatment with Levothyroxine and the monitoring process.
Population	Patients aged 80 and over with a diagnosis of primary hypothyroidism for at least 6 months treated with LT4, TSH levels within the local reference range and who are community dwelling. Patients with previous diagnosis of thyroid cancer, inability to provide informed consent, and for which there was risk for the researchers to visit at their home were excluded. n=18; Male: 5 (27.8%), Female: 13 (72.2%); median age: 83 years (range 80-93 years); median length of diagnosis of hypothyroidism: 14 years (range 3-24 years); n=11 Accepters, n= 7 Decliners
Setting	Participants were approached after agreeing to randomisation on the SORTED 1a RCT ('Accepters') or from a group of patients who had declined the trial ('Decliners')
Study design	Qualitative semi-structured interview study
Methods and analysis	Semi-structured (face to face) interviews were conducted by the primary researcher (LI) between November 2012 and December 2013. Participants were interviewed individually or with a significant other present such as spouse or adult offspring. One interview was conducted in a hospital Out-patient department at the patient's request and the others were held at participant's homes. Interviews

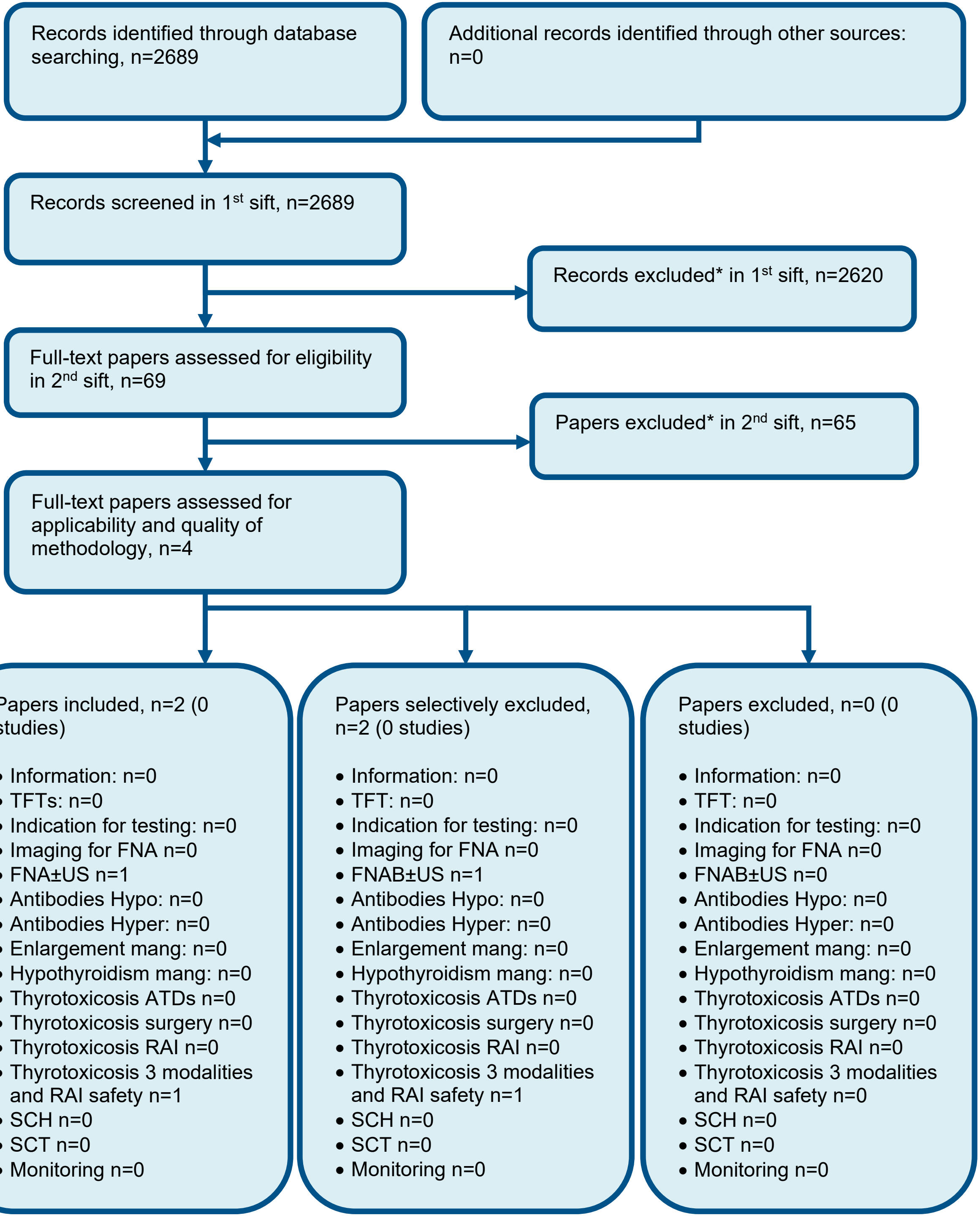
Study	Ingoe 2018 [6]
	were completed within 4 weeks of accepting or declining trial participation to help with recall and Accepters had a further interview once RCT participation had ended in order to reflect upon trial involvement. Interviews lasted on average 35 minutes. They were deliberately kept short and had a conversational style to maintain the patient's focus and prevent fatigue. A topic guide was followed with open-ended, neutral and sensitive questions that primarily explored patient's reasons for agreeing and declining to participate (in the SORTED 1a RCT). It also included questions about diagnosis, symptoms, elements of self-management and treatment with LT4. Questions were informed by a review of relevant literature. Patients' narratives in response to these questions were typically embedded within their experience of living with hypothyroidism. Areas of discussion brought up by the patients were then examined in greater depth. Interviews were audio recorded and transcribed verbatim. Thematic analysis was used to analyse interview transcripts. LI became immersed in the data by conducting and transcribing the interviews and reading through the manuscripts and reflexive notes. Emergent themes were discussed in depth with 2 fellow researchers (SH and TR) and agreement was high. A coding frame was developed to organise the data into meaningful groups. Themes were identified as the aspects of data that captured something new or important in relation to the older person's experience of hypothyroidism. Formal analysis used open and focused coding, constant comparison, deviant case analysis and memoing. Codes were added or revised as new themes and sub-themes became apparent. The transcripts were annotated with these codes. Interviews continued until data saturation was reached and no new themes were emerging. All transcripts were reviewed by SH. Preliminary findings were discussed during regular team meetings that included a patient and public involvement member, and clinical representatives working in primary and secondary care managing patients with hypothyroidism. A thematic chart using EXCEL package provided an overview of the entire data set. The chart was organised into three themes. The credibility of the analysis was agreed upon by LI, SH and TR. Patient quotes were used to illustrate the themes. Grounded theory approach was also used. Emergent themes were mapped to dimensions of the Health Belief Model (HBM: Perceived seriousness, perceived susceptibility, perceived benefits and perceived barriers) and the Healthy Ageing Model, to aid interpretation and application of the interview findings. The former model states that health behaviour is determined by personal beliefs or perceptions about disease and the strategies used to reduce its occurrence. The latter focuses on active engagement in health care for older adults with chronic health conditions managed in primary care and provides a framework to guide healthcare professionals in delivering supported self-management.
Findings	1. **Investigation**
	a. Symptoms: The findings suggest significant gaps in older participants' knowledge and understanding of the condition and its symptoms Participants appeared to believe that hypothyroidism is relatively symptom free. Symptoms were described as being few in number and were commonly attributed to other causes, demonstrating participants' uncertainty about the relationship of known common or classic symptoms to hypothyroid diagnosis. Participants rarely discussed their hypothyroidism in terms of symptoms but instead tended to talk in terms of genetic predisposition or of an inevitable effect of ageing. Consequently, the impact of ongoing symptoms such as tiredness, sensitivity to the cold and those related to appearance such as thinning hair and brittle nails tended to be minimised or to be attributed to other causes such as advancing age, symptoms of weight-gain to being less active or other co-morbidities. It appeared that diagnosis may often be delayed as a consequence of GPs attributing

Study	Ingoe 2018 [6]
	symptoms to other causes, causing distress. Some participants appeared to be uncertain about the relationship of their symptoms to hypothyroidism and persisting symptoms were not perceived as problematic (in terms of their hypothyroidism) once treatment with LT4 had commenced. Patients perceived that symptoms cannot be managed by clinicians because blood test results are within normal parameters indicating they are in a euthyroid state, which in turn lowers patients' perceived susceptibility to the condition, making them less likely to adopt healthier behaviours to lessen their impact. None of the participants appeared to associate management with symptom checks but rather with blood samples. According to the HBM patients' disconnection between on-going symptoms and the stability of their hypothyroidism may inhibit them acting on manifest symptoms as 'cues to action' to improve the management of ongoing symptoms.
	b. Diagnosis: The circumstances surrounding diagnosis appeared to be sometimes vague. Patients often perceived that the presence of the condition is determined by blood tests, regardless of the presence of manifest symptoms. Findings suggested that participants' initial experience of receiving a diagnosis and whether or not the diagnosis came about following significant manifest symptoms or was an incidental finding following what appeared to them as a routine blood test, may influence their perceived severity of hypothyroidism, which in turn may influence their health behaviour. The circumstances surrounding diagnosis, influenced participants' beliefs about the presence of disease, with some questioning the need for medication and others demonstrating an expectation that a reduction in LT4 dose would ultimately results in a return of symptoms.
	2. Treatment/Management
	a. Biochemical management: Some participants believed that LT4 is an essential and beneficial medication although the 'silent' nature of hypothyroidism had caused others to doubt the veracity of the diagnosis or to question the need to continue to take thyroid replacement treatment. The number and type of prescribed medicines can create everyday anxieties. For example participants worry that they may take the wrong dose or the wrong tablet. By understanding prescribed medication and its use, older people could assume responsibility and contribute to decisions in relation to their healthcare.
	b. Dose adjustments: There was a tendency among participants to view increases in LT4 doses during long term treatment as an advantageous event. Often participants had been explicitly told that an increase would have direct health benefits. Patients' past experience and sense of coherence shows that as they age they tend to take more medication for other comorbidities and the dosage of medication also increases. Although participants state that they are not concerned about a change in LT4 dose on their health status, they assume that they would feel worse if the dose was reduced. Participants describe a tendency to receive limited explanations of the reasons for altering LT4 dosage and little or no autonomy in decision-making and control over LT4 dosage. Lack of information sharing, including being unsure about why the dose of LT4 would be altered, seems to either cast doubt on the diagnosis of hypothyroidism or the necessity of taking medication or lead to passive acceptance. Consequently some participants seek out information from informal sources to fully understand diagnostic decisions and treatment changes. Findings suggest that patients in this age group do want to understand hypothyroidism and its management, especially when LT4 doses are adjusted. However, they do not understand dose changes. An explanation of the relationship between biochemical markers and dosage could address this uncertainty and aid patients' understanding.
	c. Perceived benefits: are likely to influence the appropriate management or changes to the management of hypothyroidism in older patients. Patients who perceive benefits of being on a higher dose of LT4 for the suppression of symptoms may perceive

Study	Ingoe 2018 [6]
	a reduction in LT4 dose as a ‘threat’, which will in turn influence the likelihood of them being receptive to a reduction in dose.
	d. Perceived barriers: Perceived barriers to ongoing management appear to be a lack of understanding of hypothyroidism and the significance of TSH levels and their relationship to LT4 doses and are likely to influence management.
Limitations and applicability of evidence	Minor limitations due to data richness and role of the researcher. Minor concerns over applicability due to study’s original aim and population limited to older adults.

Appendix E: Health economic evidence selection

Figure 2: Flow chart of health economic study selection for the guideline



Records identified through database searching, n=2689

Additional records identified through other sources: n=0

Records screened in 1st sift, n=2689

Records excluded* in 1st sift, n=2620

Full-text papers assessed for eligibility in 2nd sift, n=69

Papers excluded* in 2nd sift, n=65

Full-text papers assessed for applicability and quality of methodology, n=4

Papers included, n=2 (0 studies)

- Information: n=0
- TFTs: n=0
- Indication for testing: n=0
- Imaging for FNA n=0
- FNA±US n=1
- Antibodies Hypo: n=0
- Antibodies Hyper: n=0
- Enlargement mang: n=0
- Hypothyroidism mang: n=0
- Thyrotoxicosis ATDs n=0
- Thyrotoxicosis surgery n=0
- Thyrotoxicosis RAI n=0
- Thyrotoxicosis 3 modalities and RAI safety n=1
- SCH n=0
- SCT n=0
- Monitoring n=0

Papers selectively excluded, n=2 (0 studies)

- Information: n=0
- TFT: n=0
- Indication for testing: n=0
- Imaging for FNA n=0
- FNAB±US n=1
- Antibodies Hypo: n=0
- Antibodies Hyper: n=0
- Enlargement mang: n=0
- Hypothyroidism mang: n=0
- Thyrotoxicosis ATDs n=0
- Thyrotoxicosis surgery n=0
- Thyrotoxicosis RAI n=0
- Thyrotoxicosis 3 modalities and RAI safety n=1
- SCH n=0
- SCT n=0
- Monitoring n=0

Papers excluded, n=0 (0 studies)

- Information: n=0
- TFT: n=0
- Indication for testing: n=0
- Imaging for FNA n=0
- FNAB±US n=0
- Antibodies Hypo: n=0
- Antibodies Hyper: n=0
- Enlargement mang: n=0
- Hypothyroidism mang: n=0
- Thyrotoxicosis ATDs n=0
- Thyrotoxicosis surgery n=0
- Thyrotoxicosis RAI n=0
- Thyrotoxicosis 3 modalities and RAI safety n=0
- SCH n=0
- SCT n=0
- Monitoring n=0

* Non-relevant population, intervention, comparison, design or setting; non-English language
TFT; thyroid function test, FNA; fine-needle aspiration, US; ultrasound, RAI; radioactive iodine, ATDs; antithyroid drugs, Mang; management, SCH; Subclinical hypothyroidism, SCT; Subclinical thyrotoxicosis.

Appendix F: Health economic evidence tables

None

Appendix G: Health economic analysis

None

Appendix H: Excluded studies

H.1 Excluded qualitative studies

Table 7: Studies excluded from the qualitative review

Reference	Reason for exclusion
Davies 2017[1]	Inappropriate population
Hookham 2016[4]	Abstract only
Hookham 2017[5]	Inappropriate study design
Lee 2016[7]	Inappropriate population
Razvi 2005[9]	Inappropriate study design

H.2 Excluded health economic studies

None